

SN 09/828,592

Preliminary Amendment filed July 10, 2003

Amendments to the Claims:

The following listing of claims replaces all prior versions and listings of claims in the application:

1-24 (canceled).

25. (new) A modified antithrombin protein having an H-helix, wherein at least one amino acid of the H-helix is modified to have a more positive charge than an H-helix of non-modified antithrombin.

26. (new) The modified antithrombin protein of claim 25, wherein at least one negatively charged amino acid of the non-modified H-helix is substituted with a neutral or positively charged amino acid to form the modified H-helix.

27. (new) The modified antithrombin protein of claim 25, wherein at least one neutral amino acid of the non-modified H-helix is substituted with a positively-charged amino acid to form the modified H-helix.

28. (new) The modified antithrombin protein of claim 25, wherein the at least one amino acid of the H-helix modified to have a more positive charge than an H-helix of non-modified antithrombin is in the region of amino acids 304-314.

29. (new) The modified antithrombin protein of claim 28, wherein the modified antithrombin protein has one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K, D309R, E310R, E312R, E313R.

30. (new) The modified antithrombin protein of claim 29, wherein the modified antithrombin protein has the following amino acid substitutions: D309K, E310K, E312K, E313K.

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31. (new) A pharmaceutical composition comprising the modified antithrombin protein of claim 25.
32. (new) A pharmaceutical composition comprising the modified antithrombin protein of claim 29.
33. (new) A composition comprising the modified antithrombin protein of claim 25 and a therapeutically effective amount of Factor VIII.
34. (new) The composition of claim 33, comprising a molar ratio of approximately 1:1 of said modified antithrombin to Factor VIII.
35. (new) A method for treating a coagulation factor deficiency in a patient, comprising administering to said patient an effective inhibitory amount of the modified antithrombin protein of claim 25; wherein said inhibitory amount is effective to inhibit an activity of thrombin bound to thrombomodulin (T-TM).
36. (new) The method of claim 35, wherein the inhibitory amount comprises a Protein C activation inhibitory amount of the modified antithrombin.
37. (new) The method of claim 36, wherein the inhibitory amount comprises an amount of the modified antithrombin effective to inhibit Activated Protein C degradation of one or more of Coagulation Factors V, VIII, or X.
38. (new) The method of claim 37, wherein the amount of modified antithrombin is effective to inhibit degradation of Factor VIII, thereby extending the bioavailability of Factor VIII in said patient.

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39. (new) The method of claim 38, wherein the modified antithrombin has one or more amino acids in the region of amino acids 304-314 modified to have a more positive charge than non-modified antithrombin.
40. (new) The method of claim 39, wherein the modified antithrombin has one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K, D309R, E310R, E312R, E313R.
41. (new) The method of claim 35, wherein the inhibitory amount comprises an effective procoagulant amount of the modified antithrombin.
42. (new) The method of claim 41, wherein the modified antithrombin has one or more amino acids in the region of amino acids 304-314 modified to have a more positive charge than non-modified antithrombin.
43. (new) The method of claim 42, wherein the modified antithrombin has one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K, D309R, E310R, E312R, E313R.
44. (new) The method of claim 35, wherein the coagulation factor deficiency is hemophilia and wherein the modified antithrombin has one or more amino acids in the region of amino acids 304-314 modified to have a more positive charge than non-modified antithrombin, and the composition comprises a hemophilia-treating effective amount of the modified antithrombin.
45. (new) A nucleic acid sequence encoding the modified antithrombin of claim 25.
46. (new) The nucleic acid sequence of claim 45, encoding a modified antithrombin protein having one or more amino acids in the region of amino acids 304-314 modified to carry a more positive charge than non-modified antithrombin.

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47. (new) The nucleic acid sequence of claim 46, wherein said one or more modified nucleic acid results in one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K, D309R, E310R, E312R, E313R.

48. (new) The nucleic acid sequence of claim 47, wherein said one or more modified nucleic acid results in one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K.
